or a salt thereof

wherein Xaa^1 is His or Tyr,

Xaa^2 is Trp or Leu, and

Xaa^3 is Tyr or Arg,

Provided that when Xaa^1 is Tyr and Xaa^2 is Leu, then Xaa^3 is not Arg,

which use is as a therapeutic agent for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, and other disorders of bone growth.

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12. (Once Amended) A new use for a peptide according to the sequence (SEQ ID NO: 6)

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH_2 (6)

which use is as a therapeutic agent for the treatment of osteoporosis and other disorders of bone growth.

REMARKS

Applicants submit this Amendment to indicate the insertion point for the substitute Sequence Listing filed concurrently herewith. Applicants respectfully request examination on the merits of this application.

Receipt of the initial Office Action on the merits is awaited.

Respectfully submitted,

Date 20 June 2003

By S. A. Bent

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Versions with Markings to Show Changes Made

IN THE SPECIFICATION

Please amend the Specification as follows:

Please replace the paragraphs beginning on page 2 at lines 10 and 27 with the following rewritten paragraphs, respectively:

Studies on the physiology of the hypothalamic-pituitary-gonadal axis have resulted in the recognition of gonadotropin releasing hormone (GnRH, otherwise known as luteinizing hormone releasing hormone, LHRH) as a key stimulate the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). More recently, a peptide related to GnRH has been identified, first in chickens (Miyamato, US Patent no. 4,540,513) and subsequently in humans (White et al., Proc. Natl. Acad. Sci. USA 95 305-309, 1998). This peptide has been called GnRH-II. The sequences of the two peptides (SEQ ID NOS 5 & 6, respectively) .

We have now found that GnRH-II is capable of modulating the differentiation of bone precursor cells and inducing the expansion of osteoblast populations. Accordingly, it is an object of the present invention to provide a pharmaceutical composition for the treatment of osteoporosis, which composition is [characterised] characterized by the inclusion of GnRH-II or an analogue thereof. More specifically, the composition includes a peptide according to the sequence (SEQ ID NO: 7).

Please replace the paragraph beginning on page 3 at line 20 with the following rewritten paragraph:

In the first embodiment, the invention as disclosed herein comprises a pharmaceutical composition for increasing bone mass or bone density, or for accelerating bone growth or repair. Preferably, the invention as disclosed herein comprises a pharmaceutical composition for the treatment of osteoporosis (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis). The

composition is [characterised] characterized in that it includes as an active principal a peptide according to the sequence (SEQ ID NO: 7).

Please replace the paragraphs beginning on page 5 at line 1 and 17 with the following rewritten paragraphs, respectively:

In a second embodiment, the invention disclosed herein comprises a method for the preparation of a pharmaceutical composition for the treatment of osteoporosis (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis) or another disorder, which method comprises the mixing of a peptide according to the sequence (SEQ ID NO: 7).

In the third embodiment, the invention as disclosed herein comprises a method for the treatment of an individual suffering from osteoporosis (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis) or another bone disorder, or considered to be at risk of so suffering. This method of treatment comprises the administration to said individual of a therapeutically effective amount of a composition containing, as an active principal, a peptide according to the sequence (SEQ ID NO: 7).

Please replace the paragraph beginning on page 8 at line 7 with the following rewritten paragraph:

1A. Preparation of resin-bound protected peptide (SEQ ID NO: 8).

Please replace the paragraph beginning on page 9 at line 22, with the following rewritten paragraph:

1B. Cleavage and deprotection (SEQ ID NO: 6).

Please replace the paragraph beginning on page 12 at line 31 with the following rewritten paragraph:

Expression of GnRH-I and GnRH-II was determined by RT-PCR using PCR primers outlined in SEQ ID NOS 1-4. The integrity of the cDNA generated was determined by assessing the relative level of actin amplification.

IN THE CLAIMS:

Please amend claims 1, 3, 5, 7, 8, 10, 11 and 12 as follows:

1. (Once Amended) A pharmaceutical composition for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, and other disorders of bone metabolism, or for accelerating bone growth or repair, which composition is [characterised] characterized by the inclusion of a peptide (SEQ ID NO: 7).

3. (Once Amended) The pharmaceutical composition according to Claim 1, wherein the peptide (SEQ ID NO: 6) is

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH_2 (6)

5. (Once Amended) A method of preparing a pharmaceutical composition for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, or another disorder of bone growth, which method comprises the mixing of a peptide according to the sequence (SEQ ID NO: 6).

7. (Once Amended) The method of Claim 5, wherein the peptide is (SEQ ID NO: 6)

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH_2 (6)

8. (Once Amended) A method of treatment of an individual suffering from osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone

status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, or another disorder of bone growth, or at risk of so suffering, which comprises the administration to said individual of a therapeutically effective amount of a pharmaceutical composition which includes a peptide according to the sequence (SEQ ID NO: 7).

10. (Once Amended) The method of Claim 8, wherein the peptide is (SEQ ID NO: 6)

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH_2 (6)

11. (Once Amended) A new use for a peptide according to the sequence (SEQ ID NO: 7)

pyroGlu-His-Trp-Ser-**Xaa**^{1}-Gly- **Xaa**^{2}- **Xaa**^{3}-Pro-Gly-NH_2 (7)

or a salt thereof

wherein **Xaa**^{1} is His or Tyr,

Xaa^2 is Trp or Leu, and

Xaa^3 is Tyr or Arg,

Provided that when **Xaa**^{1} is Tyr and **Xaa**^{2} is Leu, then **Xaa**^{3} is not Arg,

which use is as a therapeutic agent for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, and other disorders of bone growth.

12. (Once Amended) A new use for a peptide according to the sequence (SEQ ID NO: 6)

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH_2 (6)

which use is as a therapeutic agent for the treatment of osteoporosis and other disorders of bone growth.